

Accuracy Profile : a new validation approach to improve harmonization of WFD analytical results

Introduction

In the framework of implementation of WFD, reliability and harmonization of analytical data in European countries is of high importance. Unfortunately critical characteristics of method like limit of quantification, uncertainty, recovery are estimated in very different ways in European laboratories. Despite the publication of very complete documents (Eurachem Guide, ISO 5725, AFNOR NFT 90210, ...) method validation can in practice be conducted very differently.

Important difficulties can therefore be expected in the interpretation of future data if common rules are not quickly given to laboratories. The emergence of real « fit for purpose » approach of validation which describes experimental design and not only general concepts would be a real progress.

We present a recent and very promising method of validation based on the concept of accuracy profile. This method has been developed by the SFSTP commission (French Society of Pharmaceutical Science and Technology). It could be totally adapted to QA/QC requirements of WFD.

Principles

Fit for purpose

The main objective of a validation should be to guarantee that the difference between a measured value (x) and the « true value » (μ) is inferior to a given acceptance limit λ (with a defined probability of 95% for example). This is the basis of accuracy profile approach.

Concept of total error

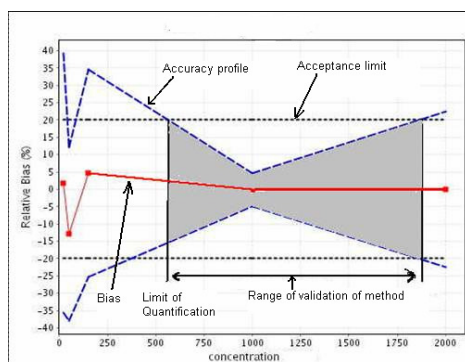
Accuracy expresses the closeness of agreement between the found value and the conventional « true » value. The closeness of agreement observed is the resultant of the sum of the systematic and random errors i.e. the total error linked to the result.

A global and visual approach

The method takes into account in a same experimental design and under intermediate conditions all the characteristics of the analytical procedure (precision, bias, calibration curve, ...). Results are gathered in a very easy and visual way in a graphic called « accuracy profile » : accuracy value in % as a function of concentration level.

Experimental design

Validation standards (samples with matrix) of known concentration and calibration standards (if calibration has to be tested) are analysed in repeatability and in reproducibility conditions. Concentration of validation standards must cover the working range of the method. A minimum of 3 concentration levels, 3 repetitions and 3 series is required. The whole standard operating procedure derived from the development of the method or applied from an ISO-CEN standard must be strictly followed.



Application : Cd in water sample by ICPMS

Experimental design

Analysis of spiked mineral water sample.

5 concentration levels : 0.5, 1, 5, 25 and 50 $\mu\text{g/l}$

3 repetitions each day. Whole procedure repeated 3 days.

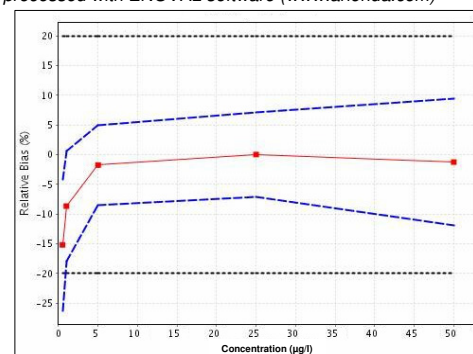
NB : this example, the concentration and the type of water are chosen for the demonstration and are not typical cases.

Accuracy profile

Profile constructed from calculated concentration and with probability 95%.

Acceptance limit arbitrarily fixed at 20% but it should be fixed at a level corresponding to a regulatory requirement or customer purpose.

NB : data are processed with ENOVAL software (www.arlenda.com)



Interpretation of profile

Validation

For the chosen acceptance limit and probability, method validated on the range 1-50 $\mu\text{g/l}$ (accuracy profile out limit for 0.5 $\mu\text{g/l}$).

Limit of quantification

Easily derived from the profile if defined as the lowest amount of analyte which can be quantitatively determined with a given accuracy (fit for purpose approach)

$\lambda = 20\% \Rightarrow \text{LOQ} = 1 \mu\text{g/l}$

$\lambda = 50\% \Rightarrow \text{LOQ} \leq 0.5 \mu\text{g/l}$

Uncertainty

Performance criteria of uncertainty 50% ($k=2$) at EQS in the context of WFD could easily be checked in a first approximation if the profile is between $-\lambda$ and $+\lambda$ at EQS level (for a complete uncertainty estimation bias should be further addressed)

Author

Ghestem Jean-Philippe

jp.ghstem@brgm.fr

Metrology, Monitoring, Analysis Dpt
BRGM

3 av Claude Guillemin

45060 ORLEANS LA SOURCE

Conclusion

For data user : this approach could assure a better quality and harmonization of data by guaranteeing that critical concepts like validation, quantification limit, estimation of uncertainty will be treated in a same way in all laboratories.

For laboratories : it is a very easy tool that gives them a clear procedure for method validation and for estimation of limit of quantification and uncertainty. However the method should be further tested on various examples (including organic analysis).

"The views expressed in this newsletter are purely those of the writer and may not in any circumstances be regarded as stating an official position of the European Commission"